Surgical ablation of atrial fibrillation with off-pump, epicardial, high-intensity focused ultrasound: Results of a multicenter trial

Jean Ninet, MD,[a] Xavier Roques, MD,[b] Rainald Seitelberger, MD,[c] Claude Deville, MD,[b] Jose Luis Pomar, MD,[d] Jacques Robin, MD, PhD,[a] Olivier Jegaden, MD,[a] Francis Wellens, MD,[e] Ernst Wolner, MD,[c] Catherine Vedrinne, MD, PhD,[a] Roman Gottardi, MD,[c] Javier Orrit, MD,[d] Marc-Alain Billes, MD,[b] Drew A. Hoffmann, PhD,[f] James L. Cox, MD,[g] and Gerard L. Champsaur, MD[f]

Extra material is available online.

Background: A simplified alternative to the Cox maze procedure to treat atrial fibrillation with epicardial high-intensity focused ultrasound was evaluated clinically, and the initial clinical results were assessed at the 6-month follow-up visit.

Methods: From September 2002 through February 2004, 103 patients were prospectively enrolled in a multicenter study. Atrial fibrillation duration ranged from 6 to 240 months (mean, 44 months) and was permanent in 76 (74%) patients, paroxysmal in 22 (21%) patients, and persistent in 5 (5%) patients. All patients had concomitant operations, and ablation was performed epicardially on the beating heart before the concomitant procedure. The device automatically created a circumferential left atrial ablation around the pulmonary veins in an average of 10 minutes, and an additional mitral line was created epicardially in 35 (34%) patients with a handheld device by using the same technology.

Results: No complications or deaths were device or procedure related. There were 4 (3.8%) early deaths and 2 late extracardiac deaths. The 6-month follow-up was complete in all survivors. At the 6-month visit, freedom from atrial fibrillation was 85% in the entire study group (80% in patients with permanent atrial fibrillation, 88% in the 35 patients who had the additional mitral line, and 100% in patients with paroxysmal atrial fibrillation). A pacemaker was implanted in 8 patients. Only the duration and type of atrial fibrillation significantly increased the risk of recurrence.

Conclusion: Epicardial, off-pump, beating-heart ablation with acoustic energy is safe and cures 80% of patients with permanent atrial fibrillation associated with long-standing structural heart disease.

From Hôpital Cardiologique Louis Pradel and Claude Bernard University,[a] Lyon, France; Hôpital Haut Lévêque and Victor Segalen University,[b] Bordeaux, France; AKH and Vienna University,[c] Vienna, Austria; Hospital Clinico and University of Barcelona,[d] Barcelona, Spain; Onze Lieve Vrouwziekenhuis,[e] Aalst, Belgium; Epicor Medical, Inc,[f] Sunnyvale, Calif; and the Division of Cardiothoracic Surgery,[g] Washington University School of Medicine, St Louis, Mo.

Received for publication Feb 6, 2005; revisions received May 7, 2005; accepted for publication May 18, 2005.

Address for correspondence: Gerard Champsaur, MD, 1430 Channing Ave, Palo Alto, CA 94301 (E-mail: gchampsaur@pacbell.net).

Address for reprints: Jean Ninet, MD, Cardiac Surgery, Hôpital Cardiologique Louis Pradel, 59 Blvd Pinel, 69003, Lyon, France (E-mail: jean.ninet@chu-lyon.fr).

J Thorac Cardiovasc Surg 2005;130:803-9

0022-5223/$30.00

doi:10.1016/j.jtcvs.2005.05.014

ET

Atrial fibrillation (AF) is a significant public health problem, affecting 2.4 million patients in the United States alone and approximately 6 million patients in the Western world and Japan. The incidence of AF increases with age with a prevalence of 4% in the population more than 60 years of age and more than 9% after 70 years of age.[1]

AF is associated with a mortality rate that is 1.5 to 2 times the expected rate in the general population after adjustment for other cardiovascular conditions,[1,2] and despite the benefits of anticoagulation, it is still responsible for thousands of strokes caused by systemic emboli with the subsequent burden on health care costs.[3,4]

The medical management of AF is well established,[2] but little was offered for the cure of AF until the direct interventional therapy of AF was initiated by Cox and colleagues[5,6] in the form of the surgical maze procedure in 1987. The Cox maze procedure remains the gold standard for the treatment of AF, with 80% to 95% freedom from AF at 15 years of follow-up.[7] Haissaguerre and colleagues[8] subse-

quently demonstrated that most individual episodes of paroxysmal AF originate from premature atrial beats located in or near the orifices of the pulmonary veins. This concept set the stage for the development of catheter-based technologies aimed at isolating the orifices of the pulmonary veins from the remainder of the left atrial wall, thereby isolating the triggers that induce AF and curing the arrhythmia.

Because of the complexity of the Cox maze procedure, several modifications have been introduced in an effort to simplify and shorten the operation. Some authors abandoned the right-sided lesions completely yet still attained AF cure rates in the range of 75% to 85%.[9,10] In addition, alternatives to the cut-and-sew techniques using various energy sources (radiofrequency, microwave, laser, and cryotherapy) have been developed in an attempt to replicate the Cox maze lines of atrial conduction block more quickly.[11-16] However, these new energy sources are all faced with similar challenges. When the energy is applied from the endocardium (either through catheters or during surgical intervention), it is impossible to determine whether the lesion is transmural. Additional energy might ensure transmurality but might also result in damage of the surrounding structures, such as the esophagus.[13,17] If these various energy sources are applied from the epicardium, their problems might be even more complex because of their thermal gradient nature. These problems include overcoming the heat-sink effect from the cooler blood (or warmer in the case of cryotherapy) and difficulty in propagating through epicardial fat. Moreover, even when applied epicardially, they can still cause damage to vital nearby structures.[18]

High-intensity focused ultrasound (HIFU) is an energy source that specifically addresses the problems associated with thermal gradient energy sources for the epicardial ablation of AF. This report details the results of the first clinical feasibility study with this new energy source in which HIFU is applied epicardially on the beating working heart without the use of cardiopulmonary bypass.

Material and Methods

Conduct of the Study

The clinical trial was a prospective multicenter study performed at 5 different institutions in 4 European countries in which 14 different surgeons participated. Identical protocols were systematically reviewed by each institutional review board and were further approved by the National Competent Authority of each country. Each enrolled patient signed an informed consent form for the procedure and for the subsequent follow-up visit, for which the physical presence of the patient at the center was required.

Patients were candidates for an Epicor Medical HIFU ablation (Epicor Medical, Inc, is a St Jude Medical company) if they had any form of AF present for at least 6 months before the operation and were already scheduled to undergo concomitant cardiac surgery for the correction of valvular, ischemic, or congenital heart disease. Exclusion criteria included acute or active infection, severe heart failure, severe progressive extracardiac disease, a prior cardiac operation, and the presence of a previously implanted intracardiac device.

The primary end point for the study was feasibility determined by the time required for sizing, insertion, and epicardial ablation by using the Epicor Medical Ablation System on the beating heart. Secondary end points included (1) safety, defined as the incidence of device-related and non–device-related complications and mortality during and 6 months after the operation, and (2) freedom from AF, atrial flutter, or both, as determined by means of surface electrocardiography (ECG) and Holter monitoring at the 6-month visit.

Device Description

The Epicor Medical Ablation System is a US Food and Drug Administration–approved, CE-marked system designed to deliver HIFU energy to ablate cardiac tissue. The system consists of the Ablation Control System (ACS) generator, a family of disposable ablation devices and a set of accessories. The ACS is a microprocessor-based unit that provides acoustic power to the ultrasound transducers.

The UltraCinch device (Figure E1) is an array of multiple ultrasound transducers that is used to produce a transmural circumferential left atrial lesion around the pulmonary vein orifices. An additional tool, the UltraWand, is a handheld ablation device with 2 transducers only for the epicardial creation of additional linear lesions.

System Characteristics

The transducers are positioned on the epicardium but separated from direct contact with the cardiac tissue by a thin perforated membrane. Room temperature normal saline is circulated between the membrane and the transducers during ablation to enhance acoustic coupling and cooling. The transducers (10×15 mm) are designed to deliver HIFU energy up to a distance of 10 mm from their surface (Figure E2), thus covering all possible thicknesses of the human left atrial free wall.[19] Beyond the focal point, the energy dissipates within the left atrial cavity without exposing the surrounding structures to potential collateral damage. The proprietary algorithm generated by the ACS uses a combination of frequency, power, and duration at which the transducers are activated and powered (from 3.8 to 6.4 MHz and from 15 to 130 W) to generate 3 sequential stages of ablation. The ablation process begins with the deep ablation stage, during which the energy is deposited distal from the transducer in the subendocardial zone, followed by the intermediate stage in which energy is deposited in the midmyocardial layer, followed by the surface stage for epicardial energy deposition. During the first 2 stages, each transducer is activated sequentially, and the energy is pulsed, whereas during the third stage, transducers are staged 3 by 3 with nonpulsed energy to eliminate any residual gap within the epicardium. Thus the lesion is built up from the endocardium back to the epicardium and is complete within approximately 10 minutes. The UltraWand is activated in a similar fashion for the creation of linear lesions during approximately 1 minute.

Surgical Technique

The ablation procedure was performed on the beating working heart before beginning the concomitant intracardiac procedure, thus avoiding additional cardiopulmonary bypass and aortic cross-clamp times. After opening the pericardium, the pericardial reflec-

TABLE 1. Patient demographic information (n = 103)

Variable	Mean	± SD	Range
Age, y	66.7	9.4	43-79
Weight, kg	72.0	13.6	44-109
Height, cm	168	10.1	143-188
AF duration, mo	44.0	53.1	6-240
LA diameter, mm	51.5	9.1	30-85
LVEF, %	61.3	10.4	36-94

SD, Standard deviation; *AF*, atrial fibrillation; *LA*, left atrium; *LVEF*, left ventricular ejection fraction.

tions around both the superior vena cava and inferior vena cava were dissected free to gain access to both the transverse and oblique sinuses. A specially designed introducer-sizer was passed behind the superior vena cava into the transverse sinus and guided into the oblique sinus and beneath the inferior vena cava, thereby completely encircling all 4 pulmonary veins. The graduated introducer-sizer was used to measure the circumference of the left atrium to select the proper size of UltraCinch and was also used to lead the UltraCinch around the left atrium. Once the introducer-sizer was removed, the 2 ends of the UltraCinch were approximated with tourniquets placed on the appropriate sutures at each end to snug the device securely around the left atrium. The ablation cycle was then initiated and progressed automatically until the cycle of ablation had been completed. During the ablation, the surgeon was free to continue with the purse strings and other preparation for the subsequent concomitant procedure. If deemed advisable, additional lesions could be created epicardially with the UltraWand, particularly the mitral line lesion extending from the pulmonary vein–encircling lesion down to the mitral valve annulus.

Patient Population

From September 2002 through February 2004, 103 patients (59 male and 44 female patients) were enrolled. AF was categorized as being permanent in 76 (74%) patients, paroxysmal in 22 (21%) patients, and persistent in 5 (5%) patients.[20] Fifty (49%) patients were 70 years of age or older, and 19 (18%) were older than 75 years (Table 1). Comorbidity was relatively common, with chronic obstructive pulmonary disease in 15 patients and renal insufficiency in 7 patients. A history of cerebral ischemia was documented in 5 patients, repeat transient ischemic attack was documented in 5 patients, and peripheral embolism was documented in 3 patients. Catheter ablation had been attempted previously in 3 patients.

Surgical intervention was conducted through a median sternotomy in 95 patients, through a ministernotomy in 5 patients, and through a limited right thoracotomy in 3 patients. A single additional mitral line was also created epicardially with the UltraWand in 35 (34%) patients. The UltraWand became available only during the last third of the study, and its use was left up to the operator's judgment. Concomitant cardiac procedures are listed in Table 2. There were no attempts to exclude the left atrial appendage.

TABLE 2. Concomitant procedures

Procedure	n = 103	%
Mitral valve surgery (2 + CABG; 32 replacements and 14 repairs)	46	44.6
Double-valve surgery (8 mitrotricuspid and 13 mitroaortic)	22	21.3
Aortic valve replacement (3 + CABG)	17	16.5
Coronary artery bypass surgery (CABG)	7	6.8
Bentall operation	6	6.8
Atrial septal defect closure	2	2
Ventricular septal defect closure (1 with pulmonary stenosis)	2	1
Triple-valve surgery	1	1

CABG, Coronary artery bypass grafting.

Postoperative Protocol

Until discharge, patients were monitored daily with standard 12-lead ECG recordings. Dictated by the type of concomitant heart disease, anticoagulant therapy was prescribed for the first postoperative week, and for the longer term, warfarin sodium (Coumadin) therapy was left to the judgment of the investigators. On the basis of previous studies, prophylactic antiarrhythmic drug therapy was recommended for at least 3 months after the operation.[8,9,14-18] External cardioversion was not encouraged in the early postoperative period.

Data were collected on standard case report forms approved by each institution's institutional review board. In addition to the demographic data collected at the preoperative visit, a standard 12-lead ECG, 24-hour Holter monitoring, and transthoracic echocardiography were performed at the time of hospital discharge and at the 3- and 6-month follow-up visits. Event-monitoring systems (Instromedix, San Diego, Calif) were required in patients with paroxysmal or persistent AF who became symptomatic between the 3- and 6-month visits. The 6-month follow-up period was completed for all 103 patients as of June 10, 2004, with no patient lost to follow-up during that period. The mean follow-up period was 177 days (median, 185 days), with a range of 2 to 232 days. Adverse events and their relatedness to the device or the procedure were collected and reviewed by each clinical investigator and the local clinical coordinator and further assessed by a clinical events committee of independent US thoracic and cardiovascular surgeons not involved in the study.

Statistical Analysis

Data were entered into a computerized database and analyzed with a statistical package (STATISTICA; StatSoft, Inc, Tulsa, Okla). The descriptive summary of data included mean ± standard deviation and 95% confidence intervals for continuous variables and proportions for categoric variables. Between-group differences were assessed with *t* tests and analysis of variance in more than 2 groups for continuous variables and χ^2 tests for nominal variables. All reported *P* values are 2 sided.

TABLE 3. Feasibility data (n = 103)

Variable	Mean	± SD	Range
Sizing time, s	47	39	9-210
Device introduction time, s	64	67	10-360
Ablation time, min	9.42	0.34	9.27-10.10
UltraCinch size (in no. of transducers)	10.3	1.4	8-13

Results

All 103 consecutive patients enrolled in the protocol were available for feasibility and safety analysis. However, in 3 patients the ablation algorithm was ended prematurely because of an ACS malfunction early in the study. Although included in the feasibility and safety analysis, these 3 patients were not expected to be free from AF and hence were not considered for the efficacy analysis.

Evaluation of Feasibility

Various aspects of the procedure were timed (Table 3). The combined time required to insert the UltraCinch device and perform the automated ablation averaged 11.9 minutes, all of which was off-pump time. During the actual ablation itself (mean time, 9.7 minutes), surgeons continued to prepare the heart for the subsequent concomitant procedure. Because this was a required part of the concomitant cardiac surgery, the AF ablation portion of the procedure added an average of only 2.2 off-pump minutes to the overall combined operative procedure. No extra time was required for epicardial fat dissection or removal.

Evaluation of Safety

No early or late complications or deaths were related to either the HIFU device or to the ablative procedure. The observed complications and mortality were characteristic in both magnitude and frequency of those commonly observed after cardiac surgery in patients with the same clinical profile undergoing the same concomitant procedures.[21]

Complications. Early complications (≤30 days after surgical intervention) occurred in 20 patients. Postoperative bleeding necessitating surgical reexploration occurred in 6 (5.8%) patients and was unrelated to the AF ablation. A permanent pacemaker was required in 5 patients. Strokes occurred between postoperative days 1 and 4 in 3 patients, but each resolved rapidly with medical therapy, with no residual effects in any patient. Two patients experienced an episode of femoral artery embolism on postoperative days 1 and 10, respectively, both of which were resolved by means of embolectomy. One patient had a serious deep wound infection (sacral decubitus ulcer) that required repeated surgical debridement. Late complications (≥30 days after surgical intervention) consisted of sinus node dysfunction requiring a permanent pacemaker in 3 patients, ventilation pneumopathy in 1 patient, delayed tamponade treated with pericardial drainage in 1 patient, and a transient ischemic attack in a patient in sinus rhythm but who was severely hypertensive.

Mortality. The operative mortality rate (30 days postoperatively) was 3.8% (n = 4), including 3 patients older than 75 years. Two patients died from left ventricular failure because of prolonged bypass and crossclamp times, and 2 other patients died from multiorgan failure after aspiration pneumonia and prolonged ventilation in one case and general sepsis caused by repeat excisions of a bed sore in the other case. Late mortality consisted of 2 patients who died from noncardiac causes: multiorgan failure in a 74-year-old man who died 2 months after a mitral valve replacement complicated by a prolonged period of assisted ventilation and bilateral pneumopathy and infection of an aortoiliac graft implanted 2 months after coronary artery bypass grafting in a severely diabetic patient.

Evaluation of Efficacy

Absence of AF or atrial flutter was evaluated in 94 patients available at the 6-month follow-up visit (excluding the 3 patients mentioned above who were not considered for the efficacy analysis and the early and late deaths). In addition to the American Heart Association/American College of Cardiology classes of AF, the surgical classes included intermittent (paroxysmal plus persistent) AF (n = 27) and continuous (permanent) AF (n = 76).[22,23] At the 6-month follow-up visit, freedom from AF was 85% in the entire study group (n = 94) and 88% in the 35 patients who received the additional mitral line. Given the late and noncontrolled introduction of the UltraWand, the study was incapable of discerning any potential added benefit of the mitral line lesion. Remarkably, in the group of 76 patients who had continuous AF with a mean duration of 52.9 months (95% confidence limit, 37.8-69 months), the freedom from AF at 6 months was 80%. Thus epicardial off-pump, beating-heart ablation performed by using an automated 10-minute algorithm with HIFU cured 80% of patients in permanent AF associated with long-standing structural heart disease requiring surgical treatment. Equally as gratifying was the observation that 100% of patients with intermittent AF were free from AF at 6 months. Two patients who were in atrial flutter at the 3-month visit underwent an external cardioversion and remained in stable sinus rhythm thereafter. There were no instances of left atrial reentrant tachycardia or left-sided flutter. Patients with intermittent AF who were free from AF at the 3-month visit were entered into an event-monitoring program. No episodes of AF or atrial flutter were documented in any of these patients between the 3- and 6-month visits.

Eight pacemakers were implanted during the follow-up period, 4 for complete heart block with normal regular atrial

TABLE 4. Comparisons between published series of surgical Maze and variants

Author	No. of patients	Surgery type	Concomitant surgery	6-mo freedom from AF
Prasad et al[7]	299	Cox III	28%	95%
Schaff et al[25]	173	Cox III	66%	80%
McCarthy et al[24]	83	Cox III	72%	90.4%
Sie et al[15]	122	Hybrid, R&L	100%	77%
Gaynor et al[27]	40	Hybrid, R&L	53%	91% (21/23)
Raman et al[26]	132	Isolated, R&L	100%	90% (45/50)
Pasic et al[11]	48	Isolated L	100%	92%
Mohr et al[13]	234	Isolated L	68%	81% (99/122)
Williams et al[12]	48	Isolated L	100%	80%
Benussi et al[14]	132	Isolated L	100%	80.5%
Knaut et al[16]	249	Isolated L	100%	65%-80%
Epicor	103	Isolated L	100%	85%-88%

R, Right-sided lesions; *L*, left-sided lesions.

activity and 4 (double chamber) for sinus node dysfunction. The assessment of left atrial function was not part of the protocol, but transthoracic pulsed Doppler echocardiography was available in a small cohort of 23 patients. All patients in sinus rhythm were documented to have left atrial contraction by the presence of a transmitral a-wave 6 months after the operation. Diastolic left ventricular function was preserved, with a peak-to-peak atrial velocity ratio of 1.90 $\pm$ 0.56, with the usual restrictions caused by the high incidence of concomitant mitral valve surgery. By using univariate analysis of preoperative and intraoperative variables, predictors for residual AF 6 months after surgical intervention were preoperative AF duration (duration of 87.4 months in patients with residual AF vs 37.06 months in patients free from AF, $P = .03$) and type of AF (freedom from AF is 80% for continuous vs 100% for intermittent, $P = .01$).

Discussion

The surgical Cox maze procedure remains the gold standard for AF ablation, with freedom from AF ranging from 80% to 97.5% over the long term in the 3 main series.[7,24,25] A major cardiac procedure to treat a functional condition, such as AF, it has not been widely adopted.

Over the past several years, the surgical treatment of AF has evolved rapidly, and a number of devices with various energy sources have been used to create linear lesions in the atria (endocardial, epicardial, or combined). These therapies have been used for both lone AF and AF associated with structural heart disease.[11-16] They have been used to replicate some or all of the lesions of the original Cox maze procedure and have evolved into something of a hybrid maze procedure that might or might not include the right-sided lesions of the original procedure (Table 4).[7,11-16,24-27] The goal of these techniques, however, is to create lines of intra-atrial conduction block that will (1) preclude the development of macroreentrant circuits in the atria, (2) isolate the trigger or triggers for AF in or near the pulmonary vein orifices, or (3) accomplish both goals 1 and 2, while at the same time allowing the atria to resume either a sinus or atrially paced rhythm. Recent clinical evidence has clearly demonstrated that the key mandatory step in the interventional treatment of AF is isolation of the pulmonary vein orifices.[10-18] Although this was a part of the original Cox maze procedure, that portion of the procedure was not designed specifically to isolate AF triggers because they were unknown at the time the Cox maze procedure was conceived and first applied.[5,6] On the contrary, since Haissaguerre and colleagues' seminal article was published in 1998,[8] virtually all subsequent lesion patterns have included isolation of the pulmonary veins.

The main advantages of HIFU over available energy sources are to provide an energy source and a method to create rapidly and off pump a reproducibly continuous and transmural lesion around the left atrium. The technology has been developed for non-blood–contacting cardiac tissue ablation from the epicardium off pump while preserving the endocardial layer, thus overcoming the challenges faced by gradient-driven technologies. The specific algorithm used to deliver acoustic energy backward from the endocardium creates a transmural lesion throughout the whole range of thicknesses of the human atrial wall. Although a number of publications describe epicardial ablation with other technologies, several steps of those procedures still require cardiopulmonary bypass and aortic crossclamp times for better exposure.[14] Moreover, epicardial fat does not need to be dissected away or removed before the ablation (Figure 1). Importantly, AF ablation was performed in 8 patients in this series through a minimally invasive approach, as described in the "Patient population" section. Finally, the unique Wand design allows for a safe epicardial creation of the mitral line also on the beating heart. The ability to ablate

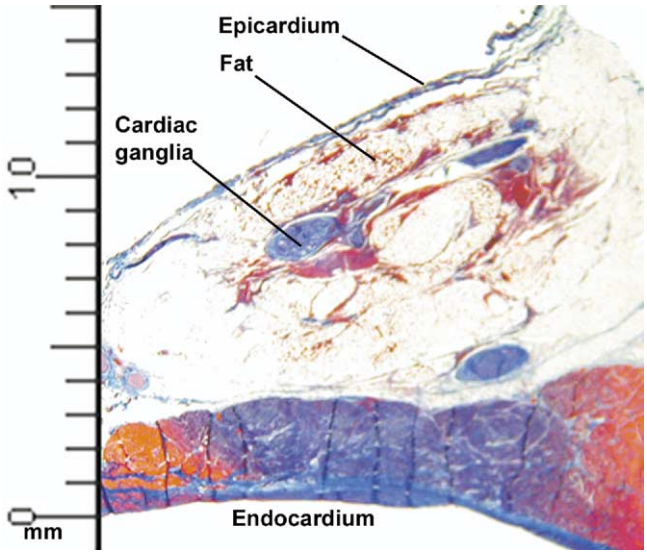

Figure 1. Histology section of bovine left atrial wall after acute ablation (Trichrome Masson staining). A fully transmural lesion (in blue) from the endocardium to the epicardium through a 10- to 12-mm wall total thickness, including 7 to 9 mm of fat tissue, is shown.

tissue surrounding coronary arteries without damaging the arteries themselves is attributed to the weak interaction between acoustic energy and blood. Ultrasound is absorbed about 30 times more strongly in soft tissue than in a low-viscosity liquid, such as blood. As a result, acoustic energy heats tissue much more than blood. The high blood flow through the coronary arteries provides a protective cooling of the endothelial lining enhanced by the absence of acoustic heating of the blood.[28]

Even though the addition of the mitral line lesion failed to significantly increase the level of efficacy, it is noticeable that there was no flutter or left atrial reentry tachycardia at 6 months, even in patients with an isolated encircling lesion. Left atrial reentry tachycardia is usually explained by persistent gaps in transmurality or continuity of the lesions or at the mitral isthmus.[9,10,15,16,23] We can, at this stage, only speculate that when using HIFU, the operator might be able to create continuously transmural lesions, to reduce the width of the mitral isthmus, and to achieve a significant degree of denervation, as documented repeatedly in our histology slides (Figure 1).

The disadvantage of the device in its current embodiment is, during the first few experiences, the perception of a certain size and rigidity, which both turn out to be very positive in that this perception does not preclude its use through a minimally invasive approach. The relative rigidity allows for a precise setting of the device on the atrial wall behind both venae cavae, without the risk of sliding toward the pulmonary veins or twisting onto itself.

Recently, the use of additional right-sided lesions has been investigated by using monopolar[15,24] or bipolar[25] radiofrequency, either as an adjunct to the traditional surgical maze procedure to replace some of the surgical lines (hybrid maze) or as an isolated procedure (Table 4). Freedom from AF ranged from 73% in long-term survivors to 90% and 91% at 6 months with a complete lesion set, including bilateral appendage resection, right-sided lesions, and adjunctive cryotherapy.[25] In this latter report, AF was paroxysmal in 63% of the patients, and along with the extensive lesion set, this might have played a role in achieving the excellent results. However, the 6-month follow-up in 2 reports[24,25] was limited to a fraction (50%) of the population under study (Table 4), and the procedure was performed during cardiopulmonary bypass and an additional aortic crossclamp time of 20 to 40 minutes.

Perhaps the only way to compare the results of this preliminary study with those in the literature is to perform a meta-analysis of the reports in which thermal lesions were performed exclusively in the left side of the heart during concomitant cardiac surgery. Although the lack of standardization in the reporting of events and results makes accurate comparisons difficult, freedom from AF at 6 months in these reported series ranges from 65% to 92% (Table 4) using either various types of radiofrequency or microwave ablation. However, except for a study reporting on a limited number of patients treated during a fully beating-heart epicardial procedure and an incomplete follow-up,[29] current ablation technology still requires significant additional cardiopulmonary bypass and aortic crossclamp times, as well as the dissection of fat when some epicardial lines are applied, and occasional serious collateral damage can still occur.[18]

Finally, the presence of thromboembolic complications raises the question of their prevention through exclusion of the left atrial appendage. The incidence of thromboembolic events after valvular surgery in this age group remains significant,[21] and the majority of patients in this report had mechanical valve replacements. At the time of the writing of the protocol, there were no studies justifying clearly the exclusion of the appendage over abstention or the advantage of an exclusion technique over another, so that the steering committee did not give a specific recommendation.

The limitations of this study are inherent in a report on the first clinical use of any technology, particularly the short follow-up period, although it was completed, with no patients lost to follow-up. Further studies will be required to assess the need for a full epicardial lesion set of the Cox maze procedure, the importance of the mitral line, the results in patients with lone AF, and the development of more minimally invasive approaches.

The contribution of the following surgeons, who participated directly in the study by training and enrolling their patients, is

greatly appreciated: Drs E. Choucroun, N. Elia, J.-P. Guibaud, N. Laborde, L. Labrousse, F. Madonna, and J.-F. Obadia.

References

1. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution and gender of patients with atrial fibrillation: analysis and implications. *Arch Intern Med.* 1995;155:469-73.
2. Prystowsky EN, Benson DW Jr, Fuster V, Hart RG, Kay GN, Myerburg RJ, et al. Management of Patients with Atrial Fibrillation. A Statement for Healthcare Professionals from the Subcommittee on Electrocardiography and Electrophysiology, American Heart Association. *Circulation.* 1996;93:1262-77.
3. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation.* 1998;98:946-52.
4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke.* 1991;22:983-8.
5. Cox JL, Schuessler RB, D'Agostino HJ Jr, Stone CM, Chang BC, Cain ME, et al. The surgical treatment of atrial fibrillation: III. Development of a definitive surgical procedure. *J Thorac Cardiovasc Surg*. 1991; 101:569-83.
6. Cox JL. The surgical treatment of atrial fibrillation: IV. Surgical technique. *J Thorac Cardiovasc Surg.* 1991;101:584-9.
7. Prasad SM, Maniar HS, Camillo CJ, Schuessler RB, Boineau JP, Sundt TM III, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. *J Thorac Cardiovasc Surg.* 2003;126:1822-8.
8. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med.* 1998;339:659-66.
9. Sueda T, Nagata H, Orihashi K, Morita S, Okada K, Sueshiro M, et al. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve operations. *Ann Thorac Surg.* 1997;63:1070-5.
10. Kalil RA, Lima GG, Leiria TL, Abrahao R, Pires LM, Prates PR, et al. Simple surgical isolation of pulmonary veins for treating secondary atrial fibrillation in mitral valve disease. *Ann Thorac Surg.* 2002;73: 1169-73.
11. Pasic M, Bergs P, Muller P, Hofmann M, Grauhan O, Kuppe H, et al. Intraoperative radiofrequency maze ablation for atrial fibrillation: the Berlin modification. *Ann Thorac Surg.* 2001;72:1484-91.
12. Williams MR, Stewart JR, Bolling SF, Freeman S, Anderson JT, Argenziano M, et al. Surgical treatment of atrial fibrillation using radiofrequency energy. *Ann Thorac Surg.* 2001;71:1939-44.
13. Mohr FW, Fabricius AM, Falk V, Autschbach R, Doll N, von Oppell U, et al. Curative treatment of atrial fibrillation with intraoperative radiofrequency ablation: short-term and midterm results. *J Thorac Cardiovasc Surg.* 2002;123:919-27.
14. Benussi S, Nascimbene S, Agricola E, Calori G, Calvi S, Caldarola A, et al. Surgical ablation of atrial fibrillation using the epicardial radiofrequency approach: mid-term results and risk analysis. *Ann Thorac Surg.* 2002;74:1050-7.
15. Sie HT, Beukema WP, Elvan A, Misier ARR. Long-term results of irrigated radiofrequency modified maze procedure in 200 patients with concomitant cardiac surgery: six years experience. *Ann Thorac Surg.* 2004;77:512-6.
16. Knaut M, Tugtekin SM, Jung F, Matschke K. Microwave ablation for the surgical treatment of permanent atrial fibrillation—a single centre experience. *Eur J Cardiothorac Surg.* 2004;26:742-6.
17. Gillinov AM, Pettersson G, Rice TW. Esophageal injury during radiofrequency ablation for atrial fibrillation. *J Thorac Cardiovasc Surg.* 2001;122:1239-40.
18. Manasse E, Medici D, Ghiselli S, Ornaghi D, Gallotti R. Left main coronary arterial lesion after microwave epicardial ablation. *Ann Thorac Surg.* 2003;76:276-7.
19. Ho SY, Sanchez-Quintana D, Cabrera JA, Anderson RH. Anatomy of the left atrium: implications for radiofrequency ablation of atrial fibrillation. *J Cardiovasc Electrophysiol.* 1999;10:1525-33.
20. Fuster V, Ryden LE, Asinger RW, Cannom DS, Crijns HJ, Frye RL, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary. *Circulation.* 2001;104:2118-50.
21. Mehta RH, Eagle KA, Coombs LP, Peterson ED, Edwards FH, Pagani FD, et al. Influence of age on outcomes in patients undergoing mitral valve replacement. *Ann Thorac Surg.* 2002;74:1459-67.
22. Cox JL. Atrial fibrillation I: a new classification system. *J Thorac Cardiovasc Surg.* 2003;126:1686-92.
23. Cox JL. Atrial fibrillation II: rationale for surgical treatment. *J Thorac Cardiovasc Surg.* 2003;126:1693-9.
24. McCarthy PM, Gillinov AM, Castle L, Chung M, Cosgrove D III. The Cox-Maze procedure: the Cleveland Clinic experience. *Semin Thorac Cardiovasc Surg.* 2000;12:25-9.
25. Schaff HV, Dearani JA, Daly RC, Orszulak TA, Danielson GK. Cox-Maze procedure for atrial fibrillation: Mayo Clinic experience. *Semin Thorac Cardiovasc Surg.* 2000;12:30-7.
26. Raman J, Ishikawa S, Storer MM, Power JM. Surgical radiofrequency ablation of both atria for atrial fibrillation: results of a multicenter trial. *J Thorac Cardiovasc Surg.* 2003;126:1357-65.
27. Gaynor SL, Diodato MD, Prasad SM, Ishii Y, Schuessler RB, Bailey MS, et al. A prospective, single-center clinical trial of a modified Cox maze procedure with bipolar radiofrequency ablation. *J Thorac Cardiovasc Surg.* 2004;128:535-42.
28. Curra F, Mourad P, Crum LA. High intensity focused ultrasound and tissue heating: the effect of nonlinear sound propagation and vessel presence. *Proc IEEE Ultrasonics Symposium.* 1998;2:1419-22.
29. Maessen JG, Nijs JFMA, Smeets JLRM, Vainer J, Mochtar B. Beating-heart surgical treatment of atrial fibrillation with microwave ablation. *Ann Thorac Surg.* 2002;74(suppl):1307S-11S.

Figure E1. Picture of the UltraCinch, which is an array of 8 to 14 ultrasonic transducers with 2 color-coded sutures at each end of the device used to secure it into position around the left atrial wall with a pair of tourniquets.

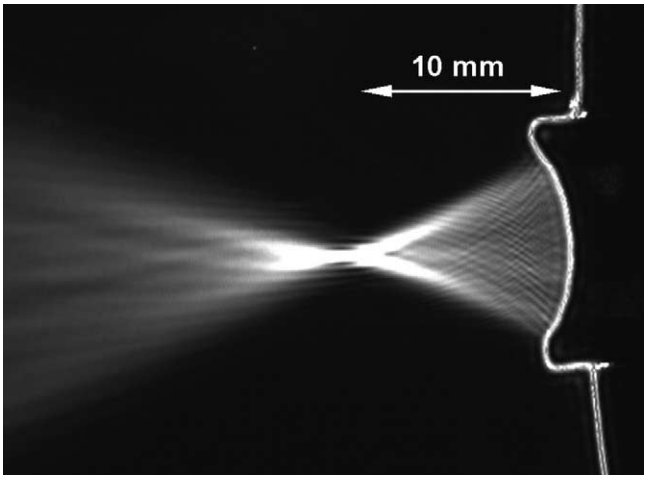

Figure E2. Focused ultrasound energy originating from the concave transducer and visualized through a Schlerein effect (fluid-phase laser illumination to visualize the ultrasonic beam). The beam converges at the focal distance and dissipates beyond that point. The focal distance is fixed and determined only by the radius of the curvature of the transducer.